Original Research

# Frequency of antibiotic use in the end-of-life cancer patients

End of life cancer patients, antibiotic use

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## Abstract

Aim: Making decisions about how to maintain general medical care and manage complications for patients in the last stage of advanced cancer is difficult. The benefits and necessity of antibiotic use in the last period of life are controversial. In this study, we aimed to investigate the frequency of antibiotic use in terminal stage cancer patients followed up with palliative care and died during their hospitalization.

Material and Methods: One hundred twenty-one patients from January 2015 to June 2020 were included.

Results: Among the 121 patients, 104 (86%) received antibiotics. Eighty-five (81.7%) patients received antibiotics until death. The mean duration of antibiotic treatment was 8.9 days. Antibiotic treatment was started 1 week before death in 88 (84.6%) of 104 patients who used antibiotics. The number of patients whose antibiotic treatment was discontinued was 3 (15.7%) in hospital wards and 16 (84.2%) in the intensive care unit.

Discussion: This is the first study on the frequency of antibiotic use in the end-of-life cancer patients in our country, and we found that the antibiotic prescription rate is high in dying cancer patients. It is questionable whether such care has positive effects on survival or quality of life. Guidelines on antibiotic use and discontinuation in patients with end-stage cancer should be developed.

Palliative care; Cancer; Death; Dying; Infectious disease; Antibiotics

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### Introduction

Making decisions about how to maintain general medical care and manage complications for patients in the last stage of advanced cancer is extremely difficult for clinicians. The goal of palliative care is to help people die with dignity, but there may come a time when treatment can do more harm than good to patients.

Infections are one of the most common causes of morbidity and mortality in cancer patients [1]. However, the clinical evidence for using or not using antibiotics in the end- of-life period is scarce, and the results are divergent [2-4]. Studies have shown that the frequency of antibiotic use in dying cancer patients varies greatly [5-7]. The use of antibiotics in dying cancer patients was found to be higher in hospitals than in hospice or palliative care centers [8-10].

Due to the lack of hospice care and the newly established palliative care centers, most of the terminal stage cancer patients still die in hospitals in our country. The aim of this study is to investigate the frequency of antibiotic use in patients with cancer in their last period of life.

## **Material and Methods**

One hundred twenty-one terminal stage cancer patients who were followed up with palliative care and died in hospital from January 2015 to June 2020 were included. The term of terminal stage was used for patients who could not receive chemotherapy, radiotherapy or surgery due to reasons such as poor performance status or disease progression, and these patients received palliative care only for symptom control. Patient's data were retrieved from medical records. Demographic data, including age, sex, primary cancer site and characteristics of infective episodes, including the site of infection, bacteriological results, use of second-line antibiotics, number of days of antibiotic use and stopping or not stopping antibiotics before death were recorded. The study was approved by the Acibadem University Ethics Committee.

## Statistical Analyses

Data were analyzed using the statistical program Statistical Package for the Social Sciences (SPSS), version 20. We reported continuous variables as mean  $\pm$  standard deviation. Categorical variables were defined as numbers (n) and percentages (%).

## Results

There were 68 men and 53 women, and the mean patient age was  $64.3\pm11.1$  (29-87 years). Patient characteristics are shown in Table 1.

Among the 121 patients, 104 (86 %) received antibiotics. The mean duration from admission to death for all patients was 9.7±7.8 (1-30) days, and the mean duration of antibiotic use was 8.93±7.5 (1-30) days. Antibiotic treatment was started 1 week before death in 88 (84.6%) of 104 patients who used antibiotics. It was found that 80 (76.9%) of these patients lived less than 14 days. Eighty-five (81.7%) patients received antibiotics until death, only 19 (18.3%) had their antibiotic treatment discontinued before death. The mean duration of antibiotic withdrawal before death was 7.3 days. The number of patients whose antibiotic treatment was discontinued was 3 (15.7%) in the hospital wards and 16 (84.2%) in the intensive

care unit. Sixty-four (52.8 %) patients died in the hospital wards, while 57 (47.1%) patients died in the intensive care unit. Culture was performed in 81 (77.8%) patients who received antibiotics. The culture was positive in 39 (48.1%) of these patients. In 18 (46.2%) patients, microorganisms were detected in blood culture, in 10 (25.6%) in urine, in 4 (10.3%) in sputum and respiratory secretions, and in 5 (12.8%) in pus. The infection episodes are shown in Table 2.

Table 1. Patient's characteristics

Total number of patients	121 (100%)
Sex	
Male/Female	68/53
Mean age: years (SD)	64.3±11.1
Primary cancer sites	
Lung	31 (25.6)
Colorectal	26 (21.5)
Pancreatic- biliary system	16 (13.2)
Upper gastrointestinal tract	12 (9.9)
Gynecological	10 (8.3)
Breast	8 (6.7)
Genitourinary	7 (5.8)
Others	11 (9)
Median number of days on the hospital (days)	9,7±7.8

**Table 2.** Infective episodes of the patients

All patients	n=104 (100%)
Site of infection	
Chest	29 (26.9)
Urinary tract	14 (13)
Gastrointestinal system	16 (14.8)
Blood	14 (13)
Skin/wound	3 (2.8)
Others/unknown	32 (29)
Bacteriological test	
Yes	81 (77.8)
No	23 (22.2)
Culture positivity	
Yes	39 (48.1)
No	42 (51.9)
Use of second-line antibiotics	
Yes	43 (41.3)
No	61 (58.7)
Antibiotic started during the last week of life	88 (84.6)
Receiving antibiotics at the end of life	85 (81.7)
Antibiotic discontinued	19 (18.3)
Mean duration of antibiotic use (days)	8,93±7.5
Outcomes	
Survived >14 days	24 (23)
Survived <14 days	60 (77)

## Discussion

The use of antibiotics in near-death cancer patients poses a dilemma. Patients with advanced cancer are more susceptible to infection [11-13]. It is not possible to predict whether antibiotics will cure or whether withholding them will result in death [8]. Currently, there is no consensus regarding the use of antibiotics for patients in palliative care, and there is still uncertainty regarding ethical and legal issues such as stopping or interrupting antibiotic treatment [11-19]. Antibiotics for terminally ill patients may have some benefits, and although limited, they also have the potential to prolong life [10,11,16]. However, even if the risks of antibiotic use are low, they can be significant for frail patients. Antibiotics can also harm patients by prolonging the dying process [20-22].

Most data on antibiotic use in end-of-life patients comes from hospices and palliative care centers, hospitals data are limited. The frequency of prescribing antibiotics varies significantly between centers, but data show that antibiotic use in hospitals is higher than hospice and palliative care centers [3,7,9]. Oneschuk et al., showed that this rate was 58% in acute care hospitals, 52% in tertiary palliative care units, and 22% in hospice [9]. However, in the teaching hospitals, 83% of individuals with cancer in their terminal hospitalization were treated with antibiotics in a review including eight studies [11]. In another study examining cancer patients who died in hospital, 86.9% of patients used antibiotics, and 35.4% of these patients continued to receive antibiotics after a transition to comfort care [7]. In this study, we found that 86% of the patients who were followed up in the hospital for palliative care used antibiotics. While this rate is higher than in hospice or palliative care units, it is similar to hospital data, in accordance with the literature.

Differences in the 'end-of-life' decisions of physicians, family members, and patients, and differences in the organization of health systems may cause differences in antibiotic use across societies towards the end of life. While it was shown that 14% of the patients who were followed up in hospice with a primary diagnosis of cancer received antibiotic treatment in the last week of life in the USA [23], this rate was found to be 85.7% in a similar study from China [5]. While some doctors are concerned that the decision to discontinue antibiotics may risk shortening the life of the patient, others worry that this therapy may prolong the death process. We determined the antibiotic withdrawal rate before death as 18.2%. This rate is lower than antibiotic withdrawal rates in hospices in Western countries. Interestingly, this ratio was 15,7% in the hospital wards and 84,2% in the intensive care unit. Explanations for the difference in antibiotics withdrawal rates in the intensive care unit are unknown.

## Study Limitations

There are several limitations to our study. First, our study was a single-centered study in a private hospital and may not reflect public hospitals practices. There are no large databases, and end-of-life care remarkably varies from hospital to hospital. Another limitation is the lack of data on decisions about using antibiotics in patients or whether they benefit from treatment. However, the main purpose of this study was not the reasons or benefit of using antibiotics.

#### Conclusion

To the best of our knowledge, this is the first study on the frequency of antibiotic use in the end-of-life cancer patients in our country.

Our study found that the antibiotic prescription rate is high in dying cancer patients. The main reasons for these high rates may be follow-up of the patients in the hospital instead of the hospice, the reluctance to stop the treatment initiated, cultural differences and the lack of guidelines on the use of antibiotics.

## Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

#### Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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#### Conflict of interest

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